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Broj: 270/15-2
Podgorica, 11.02.2021. godine

Univerzitet Crne Gore
Odbor za doktorske studije

Poštovani,

U skladu sa članom 41 i 55 Pravila doktorskih studija, u prilogu akta dostavljamo obrazac D2 uz prijedlog ovog Vijeća o imenovanju komisije za ocjenu doktorske disertacije pod nazivom "Prognostički značaj IMP3 i uticaj na preživljavanje kod pacijentkinja sa trostruko negativnim karcinomom dojke", kandidata dr med Sjekloća Nikolete, sa pratećom dokumentacijom.

S poštovanjem,

MEDICINSKI FAKULTET
D E K A N,
Prof. dr Miodrag Radunović

ISPUNJENOST USLOVA DOKTORANDA

OPŠTI PODACI O DOKTORANDU			
Titula, ime, ime roditelja, prezime	Dr med Nikoleta (Milorad) Sjekloća		
Fakultet	Medicinski fakultet UCG		
Studijski program	Medicina		
Broj indeksa	3/11		
NAZIV DOKTORSKE DISERTACIJE			
Na službenom jeziku	Prognostički značaj IMP3 i uticaj na preživljavanje kod pacijentkinja sa trostruko negativnim karcinomima dojke		
Na engleskom jeziku	Prognostic value and survival impact of IMP3 in patients with triple negative breast cancer		
Naučna oblast	Patologija		
MENTOR/MENTORI			
Prvi mentor	Prof. dr Snježana Tomić	Medicinski fakultet Sveučilište u Splitu	Patološka anatomija
Drugi mentor	(Titula, ime i prezime)	(Ustanova i država)	(Naučna oblast)
KOMISIJA ZA PREGLED I OCJENU DOKTORSKE DISERTACIJE			
Prof. dr Filip Vukmirović, predsjednik		Medicinski fakultet UCG	Patologija
Prof. dr Snježana Tomić, mentor		Medicinski fakultet Sveučilišta u Splitu	Patologija
Prof. dr Vladimir Todorović, član		Medicinski fakultet UCG	Onkologija

Datum značajni za ocjenu doktorske disertacije	
Sjednica Senata na kojoj je data saglasnost na ocjenu temu i kandidata	03.07.2018 godine
Dostavljanja doktorske disertacije organizacionoj jedinici i saglasanost mentora	02.12.2020. godine
Sjednica Vijeća organizacione jedinice na kojoj je dat predlog za imenovanje komisija za pregled i ocjenu doktorske disertacije	09.02.2021. godine

ISPUNJENOST USLOVA DOKTORANDA
U skladu sa članom 38 pravila doktorskih studija kandidat **je/nije** cjelokupna ili dio sopstvenih istraživanja vezanih za doktorsku disertaciju publikovao u časopisu sa **(SCI/SCIE)/(SSCI/A&HCI)** liste kao prvi autor.
Spisak radova doktoranda iz oblasti doktorskih studija koje je publikovao u časopisima sa (upisati odgovarajuću listu)
(dati spisak radova koji sadrži: prezimena i imena autora, naziv naučnog rada, ime izdavača, mjesto i godinu izdavanja, DOI, link ka radu i dokaz za JRC)

1. **Nikoleta Sjekloća**, Snježana Tomić, Ivana Mrkilić, Filip Vukmirović, Ljiljana Vučković, Ingrid Belas Lovasić, Marina Maras-Šimunić: Prognostic value of IMP3 immunohistochemical expression in triple negative breast cancer. Medicine 2020;99:7(e19091); http://dx.doi.org/10.1097/MD.0000000000019091. Časopis indeksiran u SCI/SCIE
   Odštapan rad dat uz obrazac.

Obrazloženje mentora o korišćenju doktorske disertacije u publikovanim radovima

U radu publikovanom u časopisu Medicine, objavljeni su rezultati iz oblasti doktorske disertacije koji se odnose na analizu ispoljenosti IMP3 biomarkera i njegov prognostički značaj kroz analizu uticaja na preživljavanje (ukupno preživljavanje i preživljavanje bez progresije bolesti) kod pacijentkinja sa trostruko negativnim karcinomom dojke. Trostruko negativni karcinom dojke karakteriše se agresivnim tokom i lošijom prognozom u odnosu na ostale tipove karcinome dojke. Takođe, ovaj tumor se karakteriše rezistentniji je na standardne hemioterapijske protokole Obzirom na navedeno, rezultatima rada, kandidat je ukazao na postojanje novog biomarkera (IMP3) koji se povećano ispoljava kod trostruko negativnih karcinoma dojke i u vezi je sa lošijom prognozom kod pacijentkinja sa ovom bolešću. Poseban doprinos ovog rada ogleda se u činjenici da određivanje IMP3 ispoljenosti omogućava sub-klasifikaciju trostruko negativnih karcinoma dojke. Pronalaskom IMP3 biomarkera kao prognostički značajnog kod TNBC, rezultati ovog rada otvaraju vrata za nova istraživanja i potencijalno pronalaženje novih terapijskih opcija koje bi ciljanjem IMP3 biomarkera unaprijedile preživljavanje i poboljšale prognozu kod ovih pacijentkinja. Odabirom metodologije koja je rutinska u kliničkoj praksi patologa, kandidat je ukazao na jednostavnost određivanja IMP3 i primjenljivost ove metode u rutinskoj kliničkoj praksi.

Datum i ovjera (pečat i potpis odgovorne osobe)

U Podgorici,
(10.02.2021. godine)

UNIVERZITET CRNE GORE MEDICINSKI FAKULTET UCG 2

MP

DEKAN
Prof. dr Miodrag Radůnović

Prilog dokumenta sadrži:

1. Potvrdu o predaji doktorske disertacije organizacionoj jedinici
2. Odluku o imenovanju komisije za pregled i ocjenu doktorske disertacije
3. Kopiju rada publikovanog u časopisu sa odgovarajuće liste
4. Biografiju i bibliografiju kandidata
5. Biografiju i bibliografiju članova komisije za pregled i ocjenu doktorske disertacije sa potvrdom o izboru u odgovarajuće akademsko zvanje i potvrdom da barem jedan član komisije nije u radnom odnosu na Univerzitetu Crne Gore

CRNA GORA - UNIVERZITET CRNE GORE
MEDICINSKI FAKULTET
UCG
Broj 2017/1
Podgorica 02.12.2020 god.

POTVRDA

Potvrđuje se da je dr med Sjekloća Nikoleta predala 7 primjeraka doktorske disertacije, pod nazivom „Prognostički značaj IMP3 i uticaj na preživljavanje kod pacijentkinja sa trostruko negativnim karcinomom dojke „ dana 02.12.2020.godine i ista je zavedena pod brojem: 2017.

Potvrda se izdaje u svrhu pregleda i ocjene doktorske disrtacije.

ŠEF STUDENTSKE SLUŽBE
Sonja Vukićević
Sonja Vukićević,diplomirani pravnik

UNIVERZITET CRNE GORE
MEDICINSKI FAKULTET
Broj: 270/15
Podgorica, 10.02.2021. godine

Na osnovu člana 64 stav 1 tačka 9 Statuta Univerziteta Crne Gore, (Bilten UCG br.337/2015 i br 447/2018), člana 41 i 55 Pravila doktorskih studija, inicijalnog predloga Komisije za doktorske studije Medicinskog fakulteta broj: 2017/2 od 18.12.2020. godine i tačke 3.8 Vodiča za doktorske studije Univerziteta Crne Gore, Vijeće Medicinskog fakulteta na elektronskoj sjednici održanoj 09-10.02.2021. godine, donijelo je

O D L U K U

I

Kandidat dr med Nikoleta Sjekloća, ispunjava formalne uslove za ocjenu doktorske disertacije: „**Prognostički značaj IMP3 i uticaj na preživljavanje kod pacijentkinja sa trostruko negativnim karcinomom dojke**".

II

Predlaže se Komisija za ocjenu doktorske disertacije dr med Sjekloća Nikolete, pod navedenim nazivom: „**Prognostički značaj IMP3 i uticaj na preživljavanje kod pacijentkinja sa trostruko negativnim karcinomom dojke**" u sastavu:

1. **Prof. dr Filip Vukmirović**, redovni profesor Medicinskog fakulteta Univerziteta Crne Gore -predsjednik
2. **Prof. dr Snježana Tomić**, redovni profesor Medicinskog fakulteta Sveučilišta u Splitu- mentor
3. **prof. dr Vladimir Todorović**, redovni profesor Medicinskog fakulteta Univerziteta Crne Gore – član.

III

Komisija za ocjenu doktorske disertacije je dužna da Vijeću Medicinskog fakulteta , podnese izvještaj koji sadrži ocjenu doktorske disertacije.

Obrazloženje

Dr med Nikoleta Sjekloća je predala doktorsku disertaciju pod nazivom: „Prognostički značaj IMP3 i uticaj na preživljavanje kod pacijentkinja sa trostruko negativnim karcinomom dojke" dana 02.12.2020. godine.
Vijeće Medicinskog fakulteta je utvrdilo da kandidat ispunjava uslove iz člana 38 Pravila doktorskih studija, da kandidat dr med Sjekloća Nikoleta ima, kao prvi autor rad sa rezultatima iz teze objavljen u časopisu sa SCI/SCIE liste. Samim tim su se stekli uslovi da se imenuje Komisija za ocjenu pomenute doktorske disertacije. Na osnovu svega navedenog, odlučeno je kao u dispozitivu ove Odluke.

VIJEĆE MEDICINSKOG FAKULTETA
PREDSJEDAVAJUĆI,

Prof. dr Miodrag Radunović, dekan

Observational Study

Medicine

OPEN

Prognostic value of IMP3 immunohistochemical expression in triple negative breast cancer

Nikoleta Sjekloča, MD[a], Snjezana Tomić, MD, PhD[b,c], Ivana Mrklić, MD, PhD[b,c,*], Filip Vukmirović, MD, PhD[a,d], Ljiljana Vučković, MD, PhD[a,d], Ingrid Belas Lovasić, MD, PhD[e], Marina Maras-Šimunić, MD, PhD[f]

Abstract

Triple negative breast cancer (TNBC) account for 12% to 17% of all breast cancers. It is a heterogeneous group of tumors associated with aggressive clinical course. Insulin-like growth factor II mRNA binding protein 3 (IMP3) belongs to a family of insulin-like growth factor type II (IGF2), which plays a key role in the transmission and stabilization of mRNA, cell growth, and migration during embryogenesis. Increased expression of IMP3 is associated with aggressive behavior of different tumor types, advanced clinical stage, distant metastasis, and shorter overall survival (OS).

The study included 118 patients with breast carcinoma diagnosed as TNBC and immunohistochemical staining for estrogen receptors (ER), progesterone receptors (PR), epidermal growth factor receptor 2 (HER2/neu), Ki-67, and IMP3 was performed. Correlations between categorical variables were studied using the chi-square and the Mann–Whitney U test. For survival analysis, the Kaplan–Meier method, log-rank test and the Cox proportional hazard regression model were used.

Positive expression of IMP3 protein was present in 35.6% of TNBC. The presence of basal morphology was observed in 46.6% of TNBC. Positive IMP3 expression was connected with larger size of tumor, higher clinical stage, and basal morphology ($P=.039$, $P=.034$, $P<.001$). Disease-free survival and OS were significantly shorter in IMP3 positive TNBC.

According to results of our study IMP3 expression can be used as negative prognostic factor for triple negative breast carcinomas. Targeting IMP3 molecule could be an effective approach to the management of a triple negative breast cancer with new immunological therapies, which does not yet exist for this group of tumors.

Abbreviations: BCRP = breast cancer resistance protein, DFS = disease-free survival, EGFR = epidermal growth factor receptor, ER = estrogen receptors, HER2/neu = epidermal growth factor receptor 2, IGF2 = insulin-like growth factor type II, IMP3 = insulin-like growth factor II mRNA binding protein 3, OS = overall survival, PR = progesterone receptors, TNBC = triple negative breast cancer.

Keywords: basal morphology, IMP3, TNBC, tumor size, vascular invasion

1. Introduction

Triple negative breast cancer, accounting for 12% to 17% of all breast cancers, is a heterogeneous group of tumors associated with aggressive clinical course, blood borne liver, lung, and brain metastasis while metastases in loco regional lymph nodes are less common in comparison to other breast tumors types.[1–4] Despite good initial response to neoadjuvant chemotherapy protocols, patients with this type of tumor have higher rates of distant metastases and ultimately poor prognosis.[1,2,5] Recently, substantial efforts were made toward improving treatment outcome for TNBC patients, requiring further subclassification based on prognostic value of new molecular biomarkers.

Insulin-like growth factor II mRNA binding protein 3 (IMP3) belongs to a family of insulin-like growth factor type II (IGF2), which plays a key role in the transfer and stabilization of mRNA, cell growth, and migration during embryogenesis. To date, there are three known members of IMP3 family proteins: IMP1, IMP2, and IMP3[6] Expression of IMP3 is negative in normal, mature tissues, but was found as positive in the malignant tumors of the colon, kidney, bladder, pancreatic ductal adenocarcinoma, gastric cancer, non-small cell lung cancer, melanoma, thyroid cancer, osteosarcoma, and breast cancer and related with aggressive behavior of the tumor, advanced clinical stage, and distant metastases.[7–18]

Recent studies have shown that IMP3 expression is closely associated with estrogen receptor negativity and positive expression of EGFR.[19] IMP3 acts as a promoter of aggressive behavior in triple negative breast cancer and contributes to breast cancer chemo resistance.

IMP3 binds to breast cancer resistance protein (BCRP) mRNA and regulates BCRP expression. BCRP, also known as ATP-binding cassette super-family G member 2 , is a member of the ATP-binding cassette (ABC) transporters and a major effector of resistance to doxorubicin and mitoxantrone in breast cancer. Depletion of IMP3 expression in triple-negative breast cancer

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The authors have no funding and conflicts of interest to disclose.

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http://dx.doi.org/10.1097/MD.0000000000019091

cells increased significantly their sensitivity to doxorubicin and mitoxantrone.[20,21]

2. Materials and methods

2.1. Patients

In our study, 118 patients with triple negative breast cancer, undergoing surgery between January 2003 and December 2009, who did not receive preoperative chemotherapy and had available paraffin embedded tissue blocks were reviewed retrospectively. Clinical information was collected through the breast cancer database of the Department of Oncology and Radiotherapy, Split University Clinical Center.

All histological and Immunohistochemistry (IHC) tumor slides were evaluated by two pathologists (ST, IM) and graded according to Elston and Ellis grading method.[22] Histological types were determined according to WHO and staged according to TNM Classification.[23,24]

Ethical committee for Biomedical Research of the Clinical Hospital Center Split approved that this research are in compliance with the Helsinki Declaration (reference number 49-1/06).

2.2. Immunohistochemical analysis

Sections from fixed, paraffin embedded, cancer tissues were stained by hematoxylin/eosin with additional immunostains for ER (1:200, Dako, Glostrup, Denmark), PR (1:100, Dako), epidermal growth factor receptor 2 (HER2/neu) (HercepTest assay, Dako), Ki-67 (1:200, Dako), and IMP3 (1:150, Dako).

Immunoassays were performed on Ventana BenchMark Ultra autostainer (Roche, Tucson, AZ). HER2 status was evaluated by IHC (Hercept Test, Dako, Glostrup, Denmark) or by chromogenic in situ hybridization (SPOT-Light HER2 CISH Kit, Invitrogen/Zymed, Camarillo, CA). Tests were scored according to ASCO/CAP guidelines.[25] ER and PR were considered positive if at least 1% of the invasive tumor cell nuclei were positive (Fig. 1).[4]

IMP3 staining was evaluated semiquantitatively according to finding of Brown staining in the cytoplasm. The intensity of staining was estimated as: absent (0), weak (1), moderate (2), and strong (3) cytoplasmic staining. The percentage of stained cells was scored: 0% (0), 1% to 25% (1), 25% to 50% (2), 51% to 75% (3), and 75% to 100% (4). Based on the sum of the score obtained by evaluation of the intensity of staining and the percentage of stained cells the final sum was formed, and interpreted in the following way: 0 to 1 as negative staining, 2 to 4 as weak positive staining, and 5 to 7 as strong positive staining (Fig. 1).

Basal like (BL) morphology was considered positive if characteristic features, such as syncytial growth pattern, high-mitotic index, large central acellular/necrotic zone, pushing borders, dense lymphocytic infiltrate at the periphery of the invasive component, and the presence of metaplastic and medullary elements were present (Fig. 2).[26]

Vascular invasion was considered positive if the presence of tumor cells in endothelium confined spaces on the periphery of the tumor was found (Fig. 2).

Ki-67 was scored by counting 1000 tumor cells using the Olympus Image Analyser (magnification 400×), at the hot spots and at the periphery of the invasive component. Data are expressed as percentages of positive cells.[27]

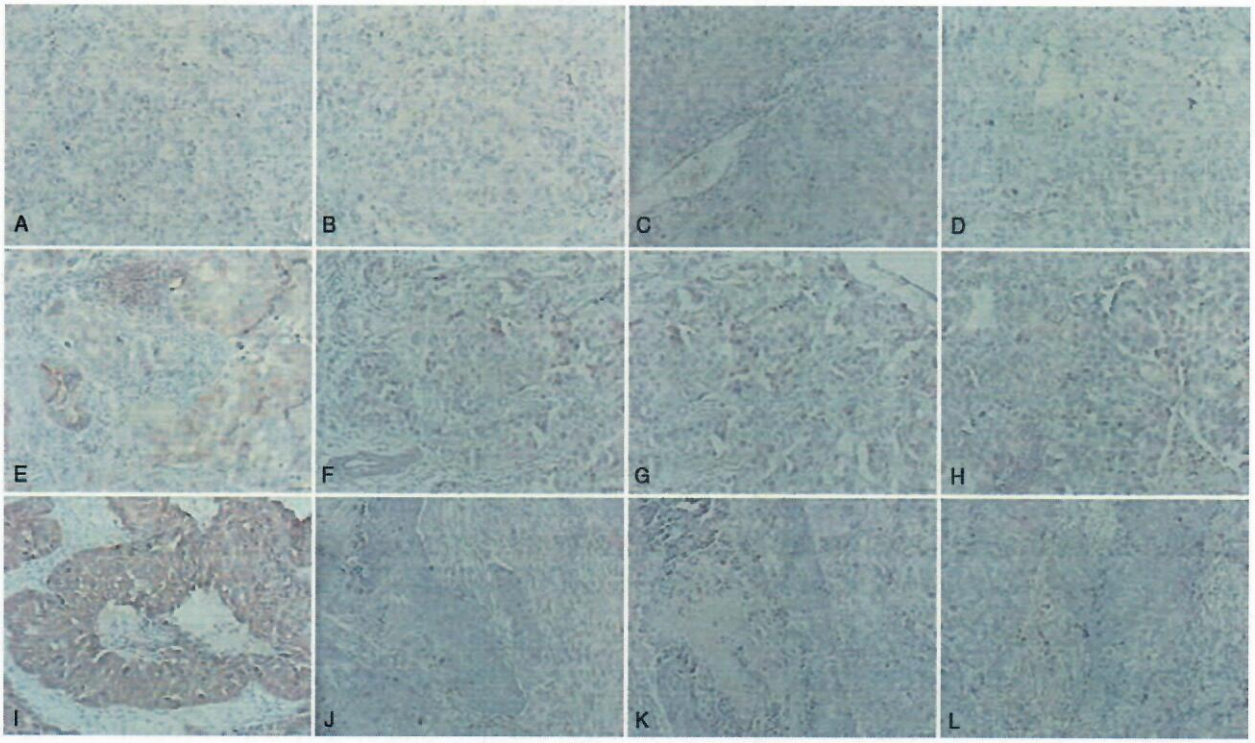

Figure 1. Immunohistochemical analysis: (A) negative IMP3 staining, (B) negative ER staining, (C) negative PR staining, (D) negative HER2 staining, (E) weak positive IMP3 staining, (F) negative ER staining, (G) negative PR staining, (H) negative HER2 staining, (I) strong positive IMP3 staining, (J) negative ER staining, (K) negative PR staining, and (L) negative HER2 staining. ER = estrogen receptors, HER2 = epidermal growth factor receptor 2, IMP3 = insulin-like growth factor II mRNA binding protein 3, PR = progesterone receptors.

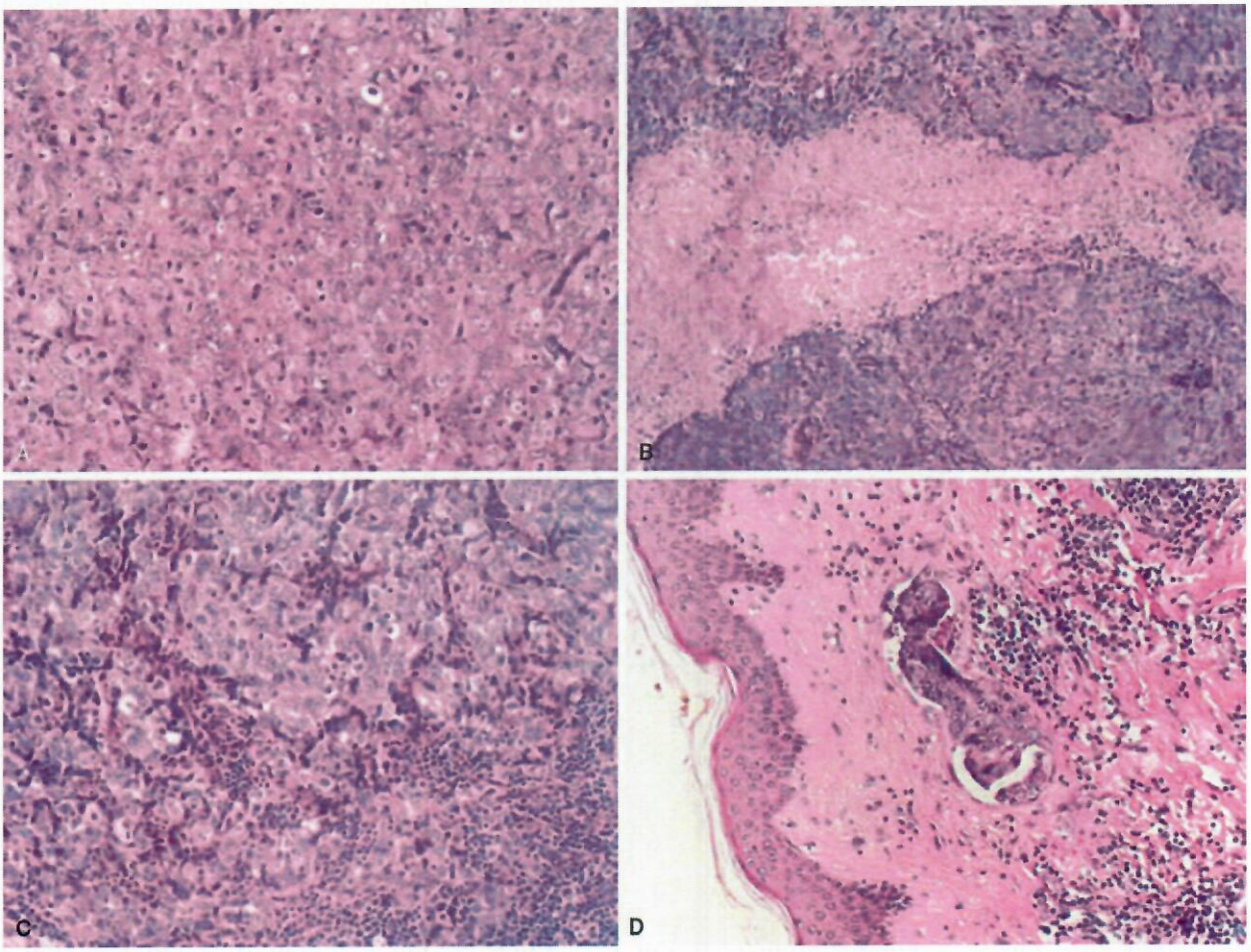

Figure 2. (A) syncytial growth pattern, (B) large central acellular/necrotic zone, (C) dense lymphocytic infiltrate at the periphery of the invasive component, and (D) vascular invasion.

2.3. Statistical analysis

Data were analyzed using Statistics for Windows Release 12.0 (Statsoft, Tulsa, OK). All *P*-values <.05 were considered statistically significant. All statistical tests were two-sided, with 95% confidence interval. Correlations between categorical variables were studied using chi-square test. For univariate analysis, survival time was analyzed by the Kaplan–Meier method and the log-rank test was used to assess differences among groups. For disease-free survival (DFS) and overall survival (OS), survival time was censored at death, if the cause was not breast cancer or if the patient was alive without relapse on March 1, 2011. For multivariate analysis Cox proportional hazard regression model was used to simultaneously examine all factors predictive of survival in univariate analysis.

3. Results

Out of 118 TNBC, 99 (83.9%) were invasive carcinomas not otherwise specified (NOS), while 19 (16.1%) were the other specific types. The majority of TNBC were histological grade 3 (80.5%). The presence of basal morphology was observed in 55 (46.6%) tumors. The presence of vascular invasion was found in 40 (33.9%) patients (Table 1).

Out of 118 TNBC 42 (35.6%) tumors showed positive expression of IMP3. Statistical significance was found regarding

Table 1

Clinicopathological features of 118 TNBC patients.

Variables	N (%)
Age (years)	57.5 (32–97)
Tumor size (cm)	2.5 (0.8–12.0)
Histological type	
NOS	99 (83.9)
Other	19 (16.1)
Clinical stage	
IA	30 (25.4)
IIA	36 (30.5)
IIB	11 (9.3)
IIIA	15 (12.7)
IIIB	4 (3.4)
IIIC	22 (18.6)
Basal morphology	
No	63 (53.4)
Yes	55 (46.6)
Histological grade	
1	0 (0.0)
2	23 (19.5)
3	95 (80.5)
Vascular invasion	
No	78 (66.1)
Yes	40 (33.9)
IMP3 staining	
Negative	76 (64.4)
Weak positive	17 (14.4)
Strong positive	25 (21.2)

IMP3 = insulin-like growth factor II mRNA binding protein 3, NOS = not otherwise specified, TNBC = triple negative breast cancer.

Table 2

Correlation between IMP3 immunoexpression and clinicopathological parameters of 118 TNBC patients.

Variable	IMP3+* N (%)	IMP3− N (%)	P
Age (years)	62 (34–97)	55 (32–85)	0.664
Tumor size (cm)	3.0 (1.2–6.0)	2.5 (0.8–12.0)	0.039*
Histological type			
NOS	34 (81.0)	65 (85.5)	0.517
Other	8 (19.0)	11 (14.5)	
Clinical stage			
IA	5 (11.9)	25 (32.9)	0.034*
IIA	11 (26.2)	25 (32.9)	
IIB	4 (9.5)	7 (9.2)	
IIIA	7 (16.7)	8 (10.5)	
IIIB	3 (7.1)	1 (1.3)	
IIIC	12 (28.6)	10 (13.2)	
Basal morphology			
No	5 (11.9)	58 (76.3)	<0.001
Yes	37 (88.1)	18 (23.7)	
Histological grade			
1	0 (0.0)	0 (0.0)	0.289
2	6 (14.3)	17 (22.4)	
3	36 (85.7)	59 (77.6)	
Vascular invasion			
No	27 (64.3)	51 (67.1)	0.757
Yes	15 (35.7)	25 (32.9)	

IMP3 = insulin-like growth factor II mRNA binding protein 3, NOS = not otherwise specified, TNBC = triple negative breast cancer.
* IMP3 positive cases include cases with strong and weak immunostaining.

Table 3

Analysis of survival Log rank test for DFS interval for the studied indicators.

Variable	Mean DFS (months)	SE	95% CI	LR	P
Age (years)					
<52	57	8	41–73	8.95	.030
52–58	94	5	84–104		
59–71	74	8	59–90		
>71	86	8	70–102		
Tumor size (cm)					
<1.5	–	–	–	3.3	.191
1.5–2.5	83	6	71–96		
2.6–3	64	10	44–84		
>3	65	9	48–83		
Histological stage					
Ductal NOS	97	7	84–110	2.5	.114
Other	80	4	71–88		
Clinical stage					
IA	87	7	74–100		<.001
IIA	97	4	89–106		
IIB	89	11	67–111	28.5	
IIIA	52	7	38–66		
IIIB	11	2	8–14		
IIIC	59	10	39–80		
Basal morphology					
No	93	4	85–101	10.35	.001
Yes	70	6	57–82		
Histological grade					
1	–	–	–	0.49	.482
2	77	9	60–94		
3	84	4	76–92		
Vascular invasion					
No	84	5	75–94	1.31	.253
Yes	75	7	61–89		
IMP3 staining					
Negative	97	3	90–103	30.61	<.001
Weak positive	64	11	42–86		
Strong positive	50	9	32–68		

DFS = disease-free survival, IMP3 = insulin-like growth factor II mRNA binding protein 3, LR = log rank, NOS = not otherwise specified.

the IMP3 expression and tumor size, clinical stage, and basal morphology ($P=.039$, $P=.034$, $P<.001$, respectively (Table 2).

Univariate survival analysis revealed that age ($P=.030$), clinical stage ($P<.001$), basal morphology ($P=.001$), and IMP staining ($P<.001$) statistically correlated with DFS (Table 3) (Fig. 3). Univariate survival analysis revealed that age ($P=0.034$), clinical stage ($P<.001$), basal morphology ($P=.001$), and IMP3 staining ($P<.001$) statistically correlated with OS (Table 4) (Fig. 4).

Multinominal analysis was performed which included all variables that yielded significant *P*-value by univariate analysis. Therefore, an independent prognostic relevance was found for tumor size, clinical stage, and IMP3 immunostaining.

Regarding DFS, statistically significant predictors were tumor size (RR=1.64, $P=.016$), clinical stage (RR=1.25, $P=.049$), and IMP3 staining (RR=2.84, $P=.001$) (Table 5). Multinomial analysis revealed that significant predictors for OS were tumor size (RR=1.60, $P=.022$) and IMP3 (RR=2.67, $P=.001$) (Table 6).

4. Discussion

TNBC represents a heterogeneous group of tumors characterized by aggressive tumor biology responsible for poor survival outcomes in comparison with other breast cancer types and lack of targeted therapies, which is creating high unmet need for better understanding of TNBC molecular nature and development of new subclassification of this disease.[28] Discovering new biomarkers with potential prognostic and predictive value may trigger development of targeted therapies and ultimately improve TNBC outcome.

In our study the most common histological type was NOS (83.9%) and basal morphology was observed in 46.6% of TNBC, which is in concordance with results of previous studies.[28–30] Out of 118 patients 42 (35.6%) had positive expression of IMP3, and this finding is in concordance with the research of Walter et al.[31]

Analysis of the relationship between IMP3 expression and histopathological parameters in our study revealed that positive IMP3 expression significantly correlated with greater tumor size, higher clinical stage and basal morphology which are clinical and pathological predictors of aggressive biologic behavior in breast cancer. The presence of vascular invasion was observed in 33.9% samples and there was no statistically significant correlation between vascular invasion and increased IMP3 expression. Mohammed et al have found that vascular invasion was more frequently present in TNBC versus non-TNBC tumors, as well in BL more than in non-BL ones.[32] In our study, survival analyses have shown no correlation between vascular invasion and OS and DFS. Possible explanation for this finding is that in this particularly aggressive type of breast cancer vascular invasion is losing its prognostic value. The vast majority (85%) of the TNBC in our study was associated with high-histologic grade, only 19.5% tumors were moderately differentiated, and none of the

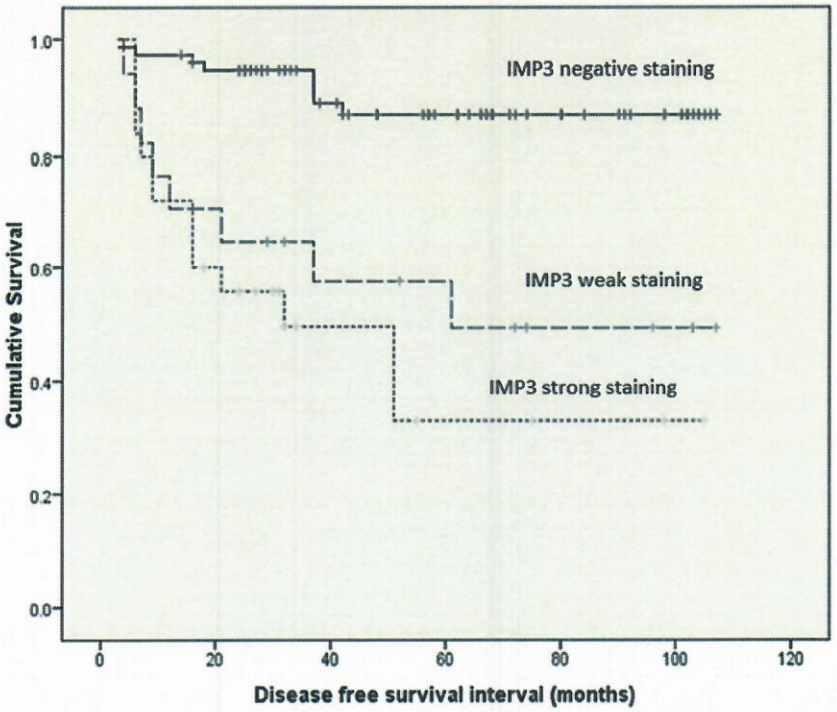

Figure 3. Kaplan–Meier curve for DFS interval for IMP3 (solid line: negative staining, dashed line: weak positive staining; dotted line: strong staining). DFS = disease-free survival, IMP3 = insulin-like growth factor II mRNA binding protein 3.

Table 4

Analysis of survival Log rank test for OS for the studied indicators.

Variable	Mean OS (months)	SE	95% CI	LR	*P*
Age (years)					
<52	59	8	43–74	8.70	.034
52–58	94	5	84–104		
59–71	75	7	61–90		
>71	87	8	71–102		
Tumor size (cm)					
<1.5	–	–	–	3.25	.197
1.5–2.5	85	6	73–96		
2.6–3	64	9	46–81		
>3	67	8	51–84		
Histological type					
NOS	97	7	83–110	2.49	.115
Other	81	4	73–89		
Clinical stage					
IA	89	6	78–101		
IIA	97	4	89–106		
IIB	87	12	63–111	28.7	<.001
IIIA	54	6	41–66		
IIIB	19	6	7–30		
IIIC	62	10	43–81		
Basal morphology					
No	94	4	86–102	10.58	.001
Yes	70	6	58–82		
Histological grade					
1	–	–	–	0.22	.637
2	80	8	64–96		
3	84	4	76–93		
Vascular invasion					
No	85	4	76–94	0.99	.320
Yes	77	7	63–90		
IMP3 staining					
Negative	97	3	91–104	30.70	<.001
Weak positive	66	10	46–87		
Strong positive	52	9	35–68		

IMP3 = insulin-like growth factor II mRNA binding protein 3, NOS = not otherwise specified, OS = overall survival.

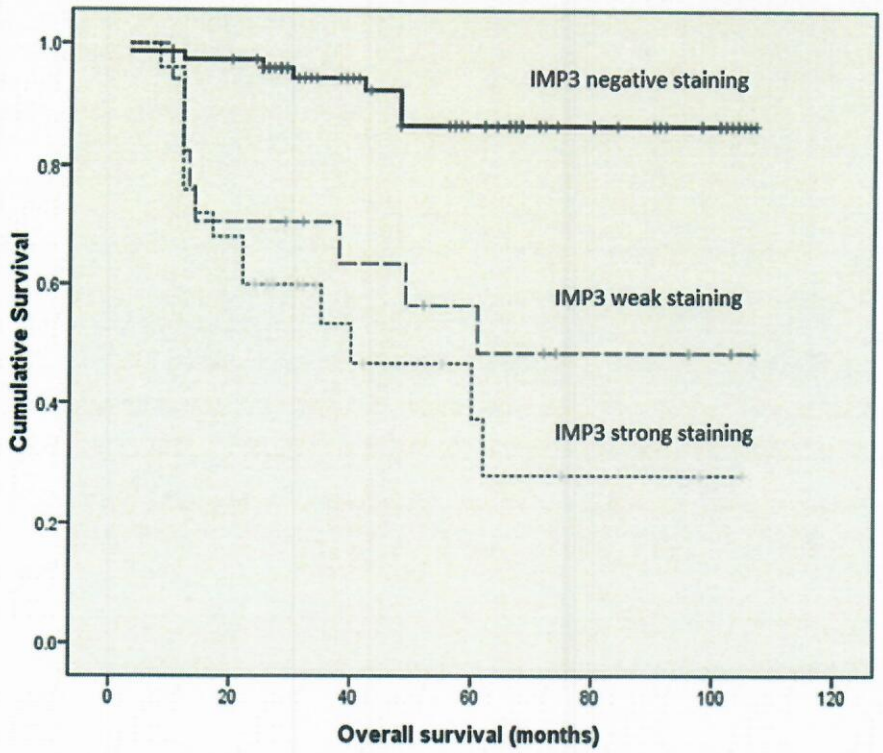

Figure 4. Kaplan–Meier curves of OS by IMP3 (solid line: negative staining; dashed line: weak positive staining; dotted line: strong staining). IMP3 = insulin-like growth factor II mRNA binding protein 3, OS = overall survival.

samples belonged to well-differentiated category, which could be the explanation for lack of correlation between IMP3 immunoexpression and histologic grade.

Survival analysis that we performed revealed that DFS interval and OS in patients with triple negative breast cancer is shorter in cases of high-clinical stage, presence of basal morphology, and strong IMP3 immunostaining. Based on the Cox regression analysis, our study showed that increased expression of IMP3 is a negative predictive factor for the prognosis of triple negative breast cancer. According to our results, determination of IMP3 biomarker, may serve as independent prognostic factor within the heterogeneous group of triple negative breast cancer. In addition, IMP3 targeting could be efficient approach for TNBC management due to several reasons: IMP3 was not expressed in

Table 5

Multinominal Cox regression analysis for DFS interval.

Variable	Referral level	RR	95% CI	P
Tumor size (cm)				
<1.5	1.5	1.64	1.10–2.46	.016
1.5–2.5				
2.6–3				
>3				
Clinical stage				
IA	IA	1.25	1.001–1.57	.049
IIA				
IIB				
IIIA				
IIIB				
IIIC				
Basal morphology				
No	No	0.66	0.21–2.08	.474
Yes				
IMP3				
Negative	Negative	2.84	1.53–5.27	.001
Weak positive				
Strong positive				

DFS = disease-free survival, IMP3 = insulin-like growth factor II mRNA binding protein 3.

Table 6

Multinominal Cox regression analysis for OS.

Variable	Referral level	RR	95% CI	P
Tumor size (cm)				
<1.5	1.5	1.60	1.07–2.39	.022
1.5–2.5				
2.6–3				
>3				
Clinical stage				
IA	IA	1.23	0.98–1.53	.071
IIA				
IIB				
IIIA				
IIIB				
IIIC				
Basal morphology				
No	No	0.74	0.24–2.22	.587
Yes				
IMP3				
Negative	Negative	2.67	1.47–4.85	.001
Weak positive				
Strong positive				

IMP3 = insulin-like growth factor II mRNA binding protein 3, OS = overall survival.

the normal tissue of the breast, the mechanism of action of this molecule is known (for the binding of sequence-specific RNA), and the inhibition of the expression of IMP3 molecule should increase the sensitivity of tumors to chemotherapy. IMP3 epitopes, based on their immunogenicity (i.e., the capacity to induce a strong and specific anti-tumor immune response), could be the target for the newly synthesized vaccine for the treatment of triple negative breast cancer.[33–35] Cancer vaccines are designed to target only cancer cells and provide sparing of surrounding healthy tissue. The results of recent clinical trials have shown their safety and almost non-existing risk of autoimmune reactivity when being tested for the treatment of lung cancers and esophageal cancers; activating IMP3 specific T-cell immune response in patients with the HLA-A 24-positive carcinoma of the esophagus and lung.[33,36,38]

It is believed that the same mechanism of IMP3 specific T cell immune response represents a new possibility for the treatment of triple negative breast cancer.

Author contributions

The work presented here was carried out in collaboration between all authors. Violeta Sjekloča and Snježana Tomić defined the research theme. Snježana Tomić and Ivana Mrklić performed pathohistological and immunohistochemical analysis and report. Filip Vukmirović, Ljiljana Vučković, Ingrid Belas Lovasić and Marina Maras-Šimunić participated in data collection and interpretation of statistical analysis. Violeta Sjekloča and Snježana Tomić performed literature review and wrote the paper. All authors were involved in drafting the manuscript or revising it critically for important intellectual content.

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1. Spisak svih radova

1. "Ne – intervencijska lokalna studija procjene bezbjednosti, podnošljivosti i efikasnosti lijeka Tocilizumab kod pacijenata sa aktivnim reumatoidnim artritisom koji su neadekvatno odgovorili na trenutnu terapiju ne-biološkim ljekovima koji utiču na tok bolesti"
2. "Praćenje bezbjednosti i podnošljivosti bevacizumaba kao druga linija tretmana pacijenata sa metastatskim kolorektalnim karcinomom nakon progresije bolesti na prethodno primijenjenu hemioterapiju"
3. "Triple Test Score in evaluation of palpable breast masses"
4. "Epidemiology of CMV infectious in Montenegro"
5. "Prognostic value of IMP3 immunohistochemical expression in triple negative breast cancer"

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O D L U K U
O IZBORU U ZVANJE

Dr FILIP VUKMIROVIĆ bira se u akademsko zvanje **redovni profesor Univerziteta Crne Gore za oblast Patologija iz Dijagnostičke grupe bazičnih medicinskih predmeta** (Patološka anatomija, osnovne studije, studijski program Medicina, Opšta patologija, osnovne studije, studijski program Stomatologija i Oralna patologija, osnovne studije, studijski program Stomatologija) **na Medicinskom fakultetu Univerziteta Crne Gore**, na neodređeno vrijeme.

SENAT UNIVERZITETA CRNE GORE
PREDSJEDNIK

Prof.dr Danilo Nikolić, rektor

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Dr Vukmirović je diplomirao na Medicinskom fakultetu Univerziteta u Prištini, 1999. godine.

Od 2000. godine, pored rada sa pacijentima, dr Vukmirović je angažovan u nastavi na studijskim programima medicine i stomatologije na Medicinskom fakultetu u Podgorici.

Zvanje specijaliste patološke anatomije je stekao 2003. godine, na Medicinskom fakultetu Univerziteta u Novom Sadu, od kada radi na Odjeljenju patologije Kliničkog centra Crne Gore.

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Autor je i koautor većeg broja naučnih radova.

2020	SCI, SCIE, SSCI, A&HCI	Nikoleta Sjekloća, Snjezana Tomic, Ivana Mrklic, Filip Vukmirovic, Ljiljana Vučkovic, Ingrid Belas Lovasic, Marina Maras-Simunic	Prognostic value of IMP3 immunohistochemical expression in triple negative breast cancer	Medicine
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2017	SCI, SCIE, SSCI, A&HCI	Vukmirović M, Bošković A, Tomašević Vukmirović I, Vujadinovic R, Fatić N, Bukumirić Z, Vukmirović F	Predictions and Outcomes of Atrial Fibrillation in the Patients with Acute Myocardial Infarction	Open medicine
2015	SCI, SCIE, SSCI, A&HCI	Milošević V., Vukmirović Filip, Zindović M., Krstić M., Milenković S., Jančić S.	Interplay between expression of leptin receptors and mucin histochemical aberrations in colorectal adenocarcinoma	Romanian journal of morphology and embryology
2015	SCI, SCIE, SSCI, A&HCI	Milošević V., Vukmirović Filip, Krstić M., Zindović M., Stojanović D., Jančić S.	Involvement of leptin receptors expression in proliferation and neoangiogenesis in colorectal carcinoma	Journal of BUON
2014	SCI, SCIE, SSCI, A&HCI	Vukmirović, F., Vukmirović, M. & Tomašević-Vukmirović, I.	Papillary fibroelastoma of the aortic valve	Vojnosanitetski pregled
2013	SCI, SCIE, SSCI, A&HCI	Vukmirović, F., Zejnilović, N., Ivović, J.	Liposarcoma of the Paratesticular Tissue and Spermatic Cord	Vojnosanitetski pregled
2013	SCI, SCIE, SSCI, A&HCI	Vukmirović, M., Angelkov, A., Vukmirović, F., Tomašević Vukmirović, I.	Successful Implantation of a Biventricular Pacing and Defibrillator Device via a Persistent Left Superior Vena Cava	Vojnosanitetski pregled
2013	SCI, SCIE, SSCI,	Radojević, N., Vukmirović, F., Čurović, I. & Šoć, M.	Asymptomatic Syphilitic Massive Necrosis of the Spleen in Late Syphilis	International Journal of STD & AIDS

	A&HCI			
2013	SCI, SCIE, SSCI, A&HCI	Vukmirović, F., Tomašević Vukmirović, I. & Vukmirović, M.	Clinicopathological Features of Ovarian Brenner Tumors in Montenegro	Central European Journal of Medicine
2013	SCI, SCIE, SSCI, A&HCI	Vukmirović, F., Vukmirović, M., Tomašević Vukmirović, I., Kavarić, P.	Renal Lipoma	Central European Journal of Medicine
2013	SCI, SCIE, SSCI, A&HCI	Vukmirović, F., Tomašević Vukmirović, I. & Vukmirović, M.	Von Meyenburg complex (hamartoma of the bile duct) mimicking liver metastases	Vojnosanitetski pregled
2012	SCI, SCIE, SSCI, A&HCI	Vujisić, S., Radulović, Lj., Knežević-Apostolski, S., Petković, S., Vukmirović, F., Apostolski, S.	Disulfiramska polineuropatija	Vojnosanitetski pregled

SVEUČILIŠTE U SPLITU
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Broj: 4-1/2
Split, 4. ožujka 2010.

Nakon provedenog natječajnog postupka, odluke Matičnog odbora za područje biomedicine i zdravstva - polje temeljnih medicinskih znanosti, kliničkih medicinskih znanosti, javnog zdravstva i zdravstvene zaštite, stomatologije i farmacije, te mišljenja stručnog povjerenstva, Fakultetsko vijeće Medicinskog fakulteta Sveučilišta u Splitu, na temelju članka 55. Statuta Sveučilišta u Splitu i članka 52. Statuta Medicinskog fakulteta u Splitu, donijelo je sljedeću

ODLUKU
O IZBORU U ZNANSTVENO-NASTAVNO ZVANJE

Prof. dr. sc. Snježana Tomić, dr. med., izabire se u znanstveno-nastavno zvanje i na radno mjesto **redovitog profesora** u Katedri za patologiju, za znanstveno područje biomedicine i zdravstva, polje kliničke medicinske znanosti, grana patologija.

Obrazloženje:

Fakultetsko vijeće Medicinskog fakulteta u Splitu odobrilo je raspisivanje natječaja za izbor jednog nastavnika u znanstveno-nastavnom zvanju redovitog profesora u Katedri za patologiju, za znanstveno područje biomedicine i zdravstva, polje kliničke medicinske znanosti, grana patologija.

Natječaj za ove poslove i radne zadatke objavljen je u službenom glasilu "Narodne novine" br. 7, dnevnom listu "Slobodna Dalmacija" i na InterNET stranici Medicinskog fakulteta 13. siječnja 2010. godine s rokom od 8 dana, a u otvorenom roku podnijela je prijavu kao jedina sudionica u natječaju prof. dr. sc.Snježana Tomić.

Matični odbor za područje biomedicine i zdravstva - polje temeljnih medicinskih znanosti, kliničkih medicinskih znanosti, javnog zdravstva i zdravstvene zaštite, stomatologije i farmacije donio je 15. veljače 2010. odluku o izboru prof. dr. sc. Snježane Tomić u znanstveno zvanje znanstvenog savjetnika, a Fakultetsko vijeće Medicinskog fakulteta u Splitu na svojoj 6. redovitoj sjednici održanoj 4. ožujka 2010. usvojilo je mišljenje stručnog povjerenstva da prof. dr. sc. Snježana Tomić ispunjava uvjete za izbor u navedeno zvanje te je donijelo odluku kao u izreci.

Sukladno čl. 102. st. 1. Zakona o znanstvenoj djelatnosti i visokom obrazovanju (NN 123/03 198/03, 105/04, 174/04 i 46/07) nastavnik se bira na znanstveno-nastavno radno mjesto redovitog profesora uz obvezu ponovnog izbora ili unaprjeđenja nakon pet godina.

Sukladno čl. 93. st. 4. istog Zakona ova Odluka stupa na snagu kad je potvrdi Senat Sveučilišta u Splitu.

Uputa o pravnom lijeku:

Protiv ove odluke može se podnijeti prigovor dekanu Medicinskog fakulteta u roku od 15 dana od njezina primitka. Prigovor se podnosi pismeno u jednom primjerku u Dekanatu Fakulteta.

Dekan:
Prof. dr. sc. Matko Marušić

Odluku dostaviti:
- Prof. dr. sc. Snježana Tomić
- Katedra za patologiju Medicinskog fakulteta u Splitu
- Senat Sveučilišta u Splitu
- Ministarstvo znanosti, obrazovanja i športa RH

REPUBLIKA HRVATSKA
NACIONALNO VIJEĆE ZA ZNANOST

Matični odbor za područje biomedicine i zdravstva
- polje temeljnih medicinskih znanosti, kliničkih medicinskih znanosti, javnog zdravstva i zdravstvene zaštite, dentalne medicine i farmacije

Klasa: 640-03/10-01/0185.
Ur.br.: 355-02-02-10-2
Zagreb, 15. veljače 2010.

Na temelju članka 35. i 95. Zakona o znanstvenoj djelatnosti i visokom obrazovanju (NN 123/03, 198/03, 105/04, 174/04, 46/07) Matični odbor za područje biomedicine i zdravstva – polje temeljnih medicinskih znanosti, kliničkih medicinskih znanosti, javnog zdravstva i zdravstvene zaštite, dentalne medicine i farmacije, na 5. sjednici održanoj 15. veljače 2010. donosi

ODLUKU
o izboru u znanstveno zvanje

Dr.sc. SNJEŽANA TOMIĆ, izvanredna profesorica Medicinskog fakulteta Sveučilišta u Splitu, izabire se u znanstveno zvanje znanstvenog savjetnika u znanstvenom području biomedicine i zdravstva – polje kliničke medicinske znanosti.

Obrazloženje

Sukladno članku 35. i 95. Zakona o znanstvenoj djelatnosti i visokom obrazovanju pristupnica se javila na natječaj koji je raspisao Medicinski fakultet Sveučilišta u Splitu za izbor u znanstveno-nastavno zvanje.

Temeljem članka 95. st. 3. Zakona o znanstvenoj djelatnosti i visokom obrazovanju, na Matičnom se odboru provodi postupak izbora u znanstveno zvanje.

Na prijedlog Stručnog povjerenstva imenovanog na sjednici Fakultetskog vijeća Medicinskog fakulteta Sveučilišta u Splitu dana 7. siječnja 2010., koje je za pristupnicu dalo svoje mišljenje o ispunjenju uvjeta iz Pravilnika o uvjetima za izbor u znanstvena zvanja – čl.1. tč.3. biomedicina i zdravstvo (NN 84/05), Fakultetsko vijeće Medicinskog fakulteta Sveučilišta u Splitu na sjednici održanoj 4. veljače 2010. utvrdilo je da pristupnica ispunjava sve uvjete za izbor u znanstveno zvanje znanstvenog savjetnika u znanstvenom području biomedicine i zdravstva – polje kliničke medicinske znanosti.

Matični odbor prihvatio je prijedlog Fakultetskog vijeća Medicinskog fakulteta Sveučilišta u Splitu te na 5. sjednici održanoj 15. veljače 2010. izabrao pristupnicu u znanstveno zvanje znanstvenog savjetnika.

POUKA O PRAVNOM LIJEKU: Protiv Odluke o izboru u znanstveno zvanje pristupnik nema pravo žalbe, ali može pokrenuti upravni spor.

REPUBLIKA HRVATSKA 4 ZAGREB NACIONALNO VIJEĆE ZA ZNANOST

Predsjednik Matičnog odbora
K. Pavelić
Prof. dr.sc. Krešimir Pavelić

Odluka se dostavlja:
1. dr.sc. Snježana Tomić
2. Medicinski fakultet u Splitu
3. Ministarstvo znanosti, obrazovanja i športa

SVEUČILIŠTE U SPLITU
UNIVERSITAS STUDIORUM SPALATENSIS

Split, 11. ožujka 2010.
Ur.broj: 01-1-42/5d-2010.

Na 42. sjednici Senata Sveučilišta u Splitu u akademskoj godini 2009./2010. održanoj dana 11. ožujka 2010. godine. pod točkom 5. d) dnevnog reda, donesena je sljedeća

ODLUKA

Na temelju čl. 93. st. 4. Zakona o znanstvenoj djelatnosti i visokom obrazovanju, a sukladno izvješću Medicinskog fakulteta u Splitu, potvrđuje se izbor dr. sc. Snježane Tomić u znanstveno-nastavno zvanje redovitog profesora – prvi izbor, za područje biomedicina i zdravstvo, polje kliničke medicinske znanosti, grana patologija, na Medicinskom fakultetu u Splitu.

REKTOR

Prof. dr. sc. Ivan Pavić

Dostaviti:
1. Medicinski fakultet u Splitu;
2. Ministarstvo znanosti, obrazovanja i športa;
3. Pismohrani.

Current Contents:

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2. Mrklic I, Pogorelic Z, Capkun V, **Tomic S.** Prognostic value of Ki-67 proliferating indeks in triple negative breast carcinomas. Pathol Res Pract 3013; 209: 296-301.
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12. Mrklic I, Bezic J, Pogorelic Z, Ilic N, Tadic T, Buljevic V, **Tomic S.** Synchronous bilateral infiltrating syringomatous adenoma of the breast. Scott Med J 2012; 57:121

13. Mrklic I, Bendic A, Kunac N, Bezic J, Forempoher G, Durdov MG, Karaman I, Prusac IK, Pisac VP, Vilovic K, **Tomic S**. Her-2/neu assesment for gastric carcinoma: validation of scoring system. Hepatogastroenterology 2012; 59: 300-3.
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Na osnovu člana 32 stav 1 tačka 14 Statuta Univerziteta Crne Gore, u vezi sa članom 29 Pravila doktorskih studija, Senat Univerziteta Crne Gore, u postupku razmatranja prijedloga Vijeća Medicinskog fakulteta br. 2188 od 11.07.2016. godine, na sjednici održanoj 27.10. 2016. godine donio je sljedeću

O D L U K U

I

Dr Snježana Tomić, redovni profesor Medicinskog fakulteta Sveučilišta u Splitu, imenuje se za **mentora** za izradu doktorske disertacije studentu doktorskih studija, **dr med. Nikoleti Sjekloća.**

II

Odluka stupa na snagu danom donošenja.

Broj: 03-2153/2
Podgorica, 27.10.2016. godine

PREDSJEDNIK SENATA

Prof. Radmila Vojvodić, rektor

3/09

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Број: 08-1742
Датум, 24.06.2015 г.

Ref:
Date,

Na osnovu člana 72 stav 2 Zakona o visokom obrazovanju (Službeni list Crne Gore br. 44/14) i člana 32 stav 1 tačka 9 Statuta Univerziteta Crne Gore, Senat Univerziteta Crne Gore, na sjednici održanoj 24. juna 2015. godine, donio je

O D L U K U
O IZBORU U ZVANJE

Dr VLADIMIR TODOROVIĆ bira se u akademsko zvanje **redovni profesor Univerziteta Crne Gore** za predmet: Osnovi kliničke onkologije na studijskom programu Medicina na Medicinskom fakultetu, na neodređeno vrijeme.

REKTOR
Prof. Radmila Vojvodić

BIOGRAFIJA

Prof. dr Vladimir Todorovic rodjen je 1964. godine u Subotici gde je zavrsio osnovno i srednje obrazovanje.

Medicinski fakultet zavrsava 1990. godine u Novom Sadu. Specijalizaciju Interne medicine polaze 1996. godine u Klinickom Centru Srbije i Univerzitetu u Beogradu, a subspecijalizaciju iz Onkologije 1998. na Institutu za onkologiju i radiologiju kao i Univerzitetu u Beogradu. Zvanje Magistra medicinskih nauka dobija 1997.,a Doktorsku disertaciju brani 2000. godine na Beogradskom Univerzitetu. Sledece godine je biran za Asistenta za predmet Onkologija Medicinskog fakulteta u Podgorici, a za docenta 2005. godine na Univerzitetu Crne Gore. Nakon toga do 2015. je bio vanredni profesor, a od te godine je redovnog profesora Univerzitet Crne Gore. Nakon staza i rada u Opstoj medicini dobija specijalizaciju iz Interne medicine i radi na Odeljenju Onkologije u Opstoj Bolnici u Subotici. Nakon zavrsene subspecijalizacije 2000. godine dobija poziv Ministarstva zdravlja Crne Gore da radi kao kadar u Klinickom Centru. Reorganizacijom Klinickog centra i osnivanjem Klinike za onkologiju i radioterapiju imenom je za prvog Direktora Klinike 2000. Godine. U periodu od 2012. do 2015. obavljao je funkciju Nacelnika Odeljenja hemioterapije. Sada se nalazi na poziciji Direktora Klinike za onkologiju i radioterapiju u Klinickom Centrtu Crne Gore. Prof. Dr Todorovic nacionalni je predstavnik Crne Gore u ESMO (Evropsko udruzenje medikalnih onkologa) od 2006. Takodje ima titulu ESMO Ambasadora. Clan je Borda direktora Mediteranskog udruzenja onkologa AROME iz Pariza sa kojim je organizovao tri medjunarodna Kursa iz Onkologije i dvije konsenzus konferencije koje imaju uticaj na regionalni razvoj dijagnostike i terapije karcinoma. Glavni je istrazivac za nekoliko klinickih studija sprovedenih u Klinickom Centru. Objavio je vise radova kao autor i koautor u casopisima na SCI listi i drugim eminentnim zurnalima. Sa saradnicima je autor udzbenika za studente Medicinskog fakulteta u Podgorici za predmet Onkologija „ Osnove klinicke onkologije i palijativna nega".

Ozenjen je i ima dvije cerke

2020	SCI, SCIE, SSCI, A&HCI	Belkacemi Y, Grellier N, Ghith S, Debbi K, Coraggio G, Bounedjar A, Samlali R, Tsoutsou PG, Ozsahin M, Chauvet MP, Turkan S, Boussen H, Kuten A, Tesanovic D, Errihani H, Benna F, Bouzid K, Idbaih A, Mokhtari K, Popovic L, Spano JP, Lotz JP, Cherif A, To H, Kovcin V, Arsovski O, Beslija S, Dzodic R, Markovic I, Vasovic S, Stamatovic L, Radosavljevic D, Radulovic S, Vrbanec D, Sahraoui S, Vasev N, Stojkovski I, Risteski M, Freixa SV, Krengli M, Radosevic N, Mustacchi G, Filipovic M, Kerrou K, Taghian AG, Todorovic V, Geara F, Gligorov J.	1. A review of the international early recommendations for departments organization and cancer management priorities during the global COVID-19 pandemic: applicability in low- and middle-income countries.	Eur J Cancer
2020	SCI, SCIE, SSCI, A&HCI	Feng Du, Wenmiao Wang, Yongsheng Wang, Ming Li, Anjie Zhu, Jiayu Wang, Ruigang Cai, Fei Ma, Ying Fan, Qing Li, Pin Zhang, Vladimir Todorovic, Peng Yuan & Binghe Xu	Carboplatin plus taxanes are non-inferior to epirubicin plus cyclophosphamide followed by taxanes as adjuvant chemotherapy for early triple-negative breast cancer	Breast Cancer Res Treat
2019	SCI, SCIE, SSCI, A&HCI	EDUARD VRDOLJAK, GYORGY BODOKY, JACEK JASSEM, RAZVAN POPESCU, ROBERT PIRKER, TANJA ČUFER, SEMIR BEŠLIJA, ALEXANDRU ENIU, VLADIMIR TODOROVIĆ, KATERINA KOPEcKOVÁ, GALIA KURTEVA, ZORICA TOMAŠEVIĆ, AGIM SALLAKU, SNEZHANA SMICHKOSKA, ŽARKO BAJIĆ, BRANIMIR SIKIC	Expenditures on Oncology Drugs and Cancer Mortality-to- Incidence Ratio in Central and Eastern Europe	Oncologist
2017	SCI, SCIE, SSCI, A&HCI	Vladimir Todorovic, Nada Cicmil Saric, Jadranka Lakicevic, Milan Sorat	Evaluation of safety of bevacizumab as second-line treatment of patients with metastatic colorectal cancer	JOURNAL OF BUON
2017	SCI, SCIE, SSCI, A&HCI	Gligorov J, Richard S, Todorovic V	New anti-HER2 agents: from second-generation tyrosine kinases inhibitors to bifunctional antibodies	Curr Opin Oncol
2017	SCI, SCIE, SSCI, A&HCI	Kandolf Sekulovic L, Peris K, Hauschild A, Stratigos A, Grob JJ, Nathan P, Dummer R, Forsea AM, Hoeller C, Gogas H, Demidov L, Lebbe C, Blank C, Olah J, Bastholt L, Herceg D, Neyns B, Vieira R, Hansson J, Rutkowski P, Krajsova	More than 5000 patients with metastatic melanoma in Europe per year do not have access to recommended first-line innovative treatments	Eur J Cancer

		I, Bylaite-Bucinskiene M, Zalaudek I, Maric-Brozic J, Babovic N, Banjin M, Putnik K, Weinlich G, Todorovic V, Kirov K, Ocvirk J, Zhukavets A, Kukushkina M, De La Cruz Merino L, Ymeri A, Risteski M, Garbe C		
2016	SCI, SCIE, SSCI, A&HCI	Vrdoljak E, Bodoky G, Jassem J, Popescu RA, Mardiak J, Pirker R, Čufer T, Bešlija S, Eniu A, Todorović V, Kubáčková K, Kurteva G, Tomašević Z, Sallaku A, Smichkoska S, Bajić Ž, Šikić BI	Cancer Control in Central and Eastern Europe: Current Situation and Recommendations for Improvement	Oncologist
2014	SCI, SCIE, SSCI, A&HCI	Todorović, V., Damjanović, S. & Lukovac Janjić, N.	Targeted therapy in metastatic hereditary Paragangliomas	Mitteilungen Klosterneuburg
2014	SCI, SCIE, SSCI, A&HCI	Todorović, V.	Prevention and management of stomatitis during treatment with Everolimus	Wulfenia
2011	SCI, SCIE, SSCI, A&HCI	Vrdoljak, E., Wojtukiewicz, MZ., Pienkowski, T., Bodoky, G., Berzinec, P., Finek, J., Todorović, V., Borojević, N., Croitoru, A. & South Eastern European Research Oncology Group	Cancer epidemiology in Central and South Eastern European countries	Croatian Medical Journal

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CRNA GORA - UNIVERZITET CRNE GORE
UCG MEDICINSKI FAKULTET
Broj 289
Podgorica 11.02. 21 god.

Uvidom u službenu evidenciju, izdaje se

P O T V R D A

Prof. dr Snježana Tomić, redovni profesor Medicinskog fakulteta Sveučilišta u Splitu, nije u radnom odnosu na Medicinskom fakultetu Univerziteta Crne Gore.

Potvrda se izdaje kao prilog obrascu D2 za kandidata dr med Sjekloća Nikoletu, i u druge svrhe se ne može koristiti.

UNIVERZITET CRNE GORE MEDICINSKI FAKULTET UCG 4

RUKOVODILAC STUDENTSKE SLUŽBE
Sonja Vukićević
Dipl. pravnik Sonja Vukićević

Vijeću Medicinskog fakulteta

Na osnovu Odluke Vijeća Medicinskog fakulteta o formiranju Komisije za doktorske studije, broj:1457 od 16.06.2015.godine, a u skladu sa tačkom 3.8 Vodiča za doktorske studije UCG - Centra za doktorske studije, nakon razmatranja ispunjavanja formalnih uslova za ocjenu doktorske disertacije i poštujući princip kompetentnosti, Komisija za doktorske studije dostavlja Vijeću Medicinskog fakulteta

INICIJALNI PRIJEDLOG
Sastava Komisije za ocjenu doktorske disertacije

I. DOKTORAND: **Dr med Sjekloća Nikoleta**

Naziv doktorske disertacije: "**Prognostički značaj IMP3 i uticaj na preživljavanje kod pacijentkinja sa trostruko negativnim karcinomom dojke**"

II. U skladu sa članom 38 Pravila doktorskih studija, doktorand dr med Sjekloća Nikoleta ispunjava uslove za ocjenu doktorske disertacije.

III. Komisija za ocjenu doktorske disertacije:

- **Prof. dr Filip Vukmirović**, redovni profesor Medicinskog fakulteta Univerziteta Crne Gore - predsjednik

- **Prof.dr Snježana Tomić**, redovni profesor Medicinskog fakulteta Sveučilišta u Splitu-mentor

- **Prof. dr Vladimir Todorović**, redovni profesor Medicinskog fakulteta Univerzatieta Crne Gore -član

KOMISIJA ZA DOKTORSKE STUDIJE

Prof. dr Filip Vukmirović

UNIVERZITET CRNE GORE

VIJEĆU MEDICINSKOG FAKULTETA

Komisiji za doktorske studije

PREDMET: Zahtjev za ocjenu doktorske disertacije

Postovani,

U skladu sa Pravilima studiranja na doktorskim studijama Univerziteta Crne Gore, ovim putem podnosim zahtjev za ocjenu doktorske disertacije pod nazivom: „Prognostički značaj IMP3 i uticaj na preživljavanje kod pacijentkinja sa trostruko negativnim karcinomom dojke".

Završetkom doktorske disertacije i objavom rada u časopisu sa SCI/SCIE liste koji sadrži djelove istraživanja sprovedenih u okviru rada na izradi doktorske disertacije, ispunila sam uslove za predaju disertacije na pregled i ocjenu, predviđene Pravilima doktorskih studija.

Ovim putem se obraćam Komisiji za doktorske studije Medicinskog fakulteta, sa molbom da inicira prijedlog Komisije za ocjenu gore navedene doktorske disertacije.

Uz Zahtjev, u prilogu dostavljam sljedeće:

- pismenu salasnost mentora
- štampani primjerak doktorske disertacije/7 primjeraka
- fotokopiju rada objavljenog kao rezultat doktorske teze
- Biografiju i bibliografiju
- CD sa cjelokupnim sadrzajem diktorske disertacije u PDF formatu i
- pisanu lzjavu o autorstvu (Prilog 1 iz Upustva o oblikovanju doktorske disertacije)

S poštovanjem,

Podnosilac Zahtjeva:

Sjekloća Nikoleta

dr Nikoleta Sjekloća

U Podgorica, datum: 02.12.2020.

Na osnovu Odluke Senata Univerziteta Crne Gore izabram sam za mentora kandidatu dr Nikoleta Sjekloća.

U fazi predaje rada za pregled i ocjenu doktorske disertacije, u skladu sa Parvilima doktorskih studija, ovim putem dajem

SAGLASNOST

Saglasna sam da kandidat dr Nikoleta Sjekloća može predati rad pod nazivom: „Prognostički značaj IMP3 i uticaj na preživljavanje kod pacijentkinja sa trostruko negativnim karcinomom dojke", na pregled i ocjenu.

Mentor:

Prof. Dr Snježana Tomić

Izjava o autorstvu

Potpisana: dr Nikoleta Sjekloća

Broj indeksa/upisa: 3/11

Izjavljujem

da je doktorska disertacija pod naslovom - Prognostički značaj IMP3 I uticaj na preživljavanje kod pacijentkinja sa trostruko negativnim karcinomom dojke

- rezultat sopstvenog istraživačkog rada,
- da predložena disertacija ni u cjelini ni u djelovima nije bila predložena za dobijanje bilo koje diplome prema studijskim programima drugih ustanova visokog obrazovanja,
- da su rezultati korektno navedeni, i
- da nijesam povrijedila autorska i druga prava intelektualne svojine koja pripadaju trećim licima.

Potpis doktoranda: Sjekloća Nikoleta

U Podgorici: 02.12.2020.

UNIVERZITET CRNE GORE
MEDICINSKI FAKULTET
MEDICINA
Broj dosijea: **3/2011**

Na osnovu člana 165 stava 1 Zakona o opštem upravnom postupku ("Službeni list RCG", broj 60/03.), člana 115 stava 2 Zakona o visokom obrazovanju ("Službeni list CG", broj 44/14.) i službene evidencije, a po zahtjevu studenta Sjekloća Milorad Nikoleta, izdaje se

UVJERENJE O POLOŽENIM ISPITIMA

Student **Sjekloća Milorad Nikoleta**, rođena **28-12-1983** godine u mjestu **Cetinje**, opština **Cetinje**, Republika **Crna Gora**, upisana je studijske **2011/2012** godine, u **I** godinu studija, kao student koji se **samofinansira** na **doktorske akademske studije**, studijski program **MEDICINA**, koji realizuje **MEDICINSKI FAKULTET** - Podgorica Univerziteta Crne Gore u trajanju od **3** (**tri**) godine sa obimom **180** ECTS kredita.

Student je položio ispite iz sljedećih predmeta:

Redni broj	Semestar	Naziv predmeta	Ocjena	Uspjeh	Broj ECTS kredita
1.	1	BIOSTATISTIKA	"A"	(odličan)	10.00
2.	1	MEDICINSKA INFORMATIKA	"A"	(odličan)	10.00
3.	1	METODOLOGIJA NAUČNOG ISTRAŽIVANJA	"B"	(vrlodobar)	10.00
4.	2	OSNOVI ĆELIJSKE BIOLOGIJE	"D"	(zadovoljavajući)	10.00
5.	2	OSNOVI IMUNOLOGIJE	"A"	(odličan)	10.00
6.	2	POČETNA ISTRAŽIVANJA	"A"	(odličan)	10.00

Zaključno sa rednim brojem **6**.

Ostvareni uspjeh u toku dosadašnjih studija je:
- srednja ocjena položenih ispita "**B**" (**9.33**)
- ukupan broj osvojenih ECTS kredita **60.00** ili **100.00%**
- indeks uspjeha **9.33**.

Uvjerenje se izdaje na osnovu službene evidencije, a u svrhu ostvarivanja prava na: (dječji dodatak, porodičnu penziju, invalidski dodatak, zdravstvenu legitimaciju, povlašćenu vožnju za gradski saobraćaj, studentski dom, studentski kredit, stipendiju, regulisanje vojne obaveze i slično).

M. P.

Broj:
Podgorica, 11.02.2021 godine

SEKRETAR,